UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,084	12/15/2003	Joseph C. Walsh	2003P88073 US	3273

28524 7590 04/09/2008

SIEMENS CORPORATION
INTELLECTUAL PROPERTY DEPARTMENT
170 WOOD AVENUE SOUTH
ISELIN, NJ 08830

EXAMINER	
KRISHNAN, GANAPATHY	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
04/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/736,084	WALSH ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 3/17/2008 has been entered.

The Request for Continued Examination filed 3/17/2008 has been carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 33-34 have been canceled.

2. Remarks drawn to rejections under 35 USC 103(a) maintained in the Final Rejection of 7/17/2007.

Claims 1-32 are pending in the case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fox et al (The Journal of Organic Chemistry, 1968, 33(4), 1592-99) in view of Miller et al (J. Org. Chem. 1963, 28, 936-41), both of record.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Fox et al teach the preparation of compound 8, a thymidine derivative (page 1593, Figure 2). This compound is structurally the same as the compounds in instant claims 21 and 30 except that the 5' hydroxyl group is protected in the instant compound. The compound of Fox has a leaving group (mesylate) as instantly claimed. The compound of Fox serves as an intermediate for making several derivatives of compound 6 that are biologically active (page 1592, right column, lines 1-5).

According to Miller et al, thymidine derivatives II (page 936, Figure 1) are also useful intermediates I the syntheses of nucleosides of potential value as antitumor agents (page 936, left column, first paragraph). Compound II of Miller is structurally very close to that of the

compound claimed in instant claim 29 except that the carbonyl group in the base is not present as an enolate. But such an enolate structure is an important intermediate as taught by Fox (above).

Fox teaches the conversion of the anhydro intermediate 4 to the derivative 5, which is the same as the compound obtained in step (c) of instant claim 1. A derivative that is structurally similar to the compound in step (a) of claim 1 (the protected derivative) is taught by Miller (structure III of Miller in Figure 1). Even though the structure of the anhydro derivatives are slightly different in both Fox and Miller one of ordinary skill in the art will recognize that the same sequence of steps can be applied to make the compound in instant claim 1 via the steps as instantly claimed with slight modifications. Such a modification based on the prior art is well within the skill level of the artisan.

Based on the teachings of the prior art, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make compounds as claimed in instant claims 21-30 via the process as claimed in instant claims 1-20 since structurally very close compounds as instantly claimed and steps for making the same are seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make compounds as instantly claimed via the process as instantly claimed and taught by the prior art, since they serve as intermediates for the syntheses of several other derivatives having biological activity including antitumor activity as taught by Fox and Miller. It is well within the purview of one of ordinary skill in the art to substitute other protecting groups and leaving groups as instantly claimed since all of these groups are well known in the art for use in such synthetic methods as instantly claimed and would extend the scope of the method.

Response to Applicants Arguments

Since Applicants have not filed any remarks/arguments with the Request for Continued Examination (filed 3/17/2008), the Examiner's response below is with regard to Applicants arguments filed 9/17/2007.

Applicants have traversed the rejection arguing that:

1. Fox et al do not teach nor suggest the instant method the purpose or the motivation for adding a hydroxyl protecting group at the 5' position of compound 8 to form the compound as recited in instant claims 29 and 31. One of skill in the art would have been motivated to use the free 5' hydroxyl compound 8 to prepare various derivatives. The intermediate compound taught by Fox is different and is used for making the tricyclic compound 6.

2. The intentional preparation of the enolate of the thymidine base such as compound 3 results in cyclization to form the tricyclic structures represented by compound 4. The compound in instant claim 29 is a methyl ether enolate that is stable and does not undergo cyclization. One of skill in the art viewing compound II of Miller and the teaching of Fox could not start with compound II of Miller and prepare the enolate of the compound of instant claim 29. There is no reasonable expectation of success.

3. The conversion of intermediate 4 to 5 in Fox is not the same as in instant claim 1.

Applicants' arguments are not found to be persuasive.

Fox et al teach the preparation of compound 8, a thymidine derivative (page 1593, Figure 2). This compound is structurally the same as the compounds in instant claims 21 and 30 except that the 5' hydroxyl group is protected in the instant compound. The compound of Fox has a leaving group (mesylate) as instantly claimed. The compound of Fox serves as an intermediate

for making several derivatives of compound 6 that are biologically active (page 1592, right column, lines 1-5). Fox may not teach the protection of the 5' hydroxyl group as recited in instant claims 29 and 31. One of skill in the art knows that protection of the hydroxyl groups in the sugar moiety is a common operation in nucleoside synthesis.

Miller teaches such protected compounds (compound II in Figure 1). According to Miller et al, thymidine derivatives II (page 936, Figure 1) are also useful intermediates in the syntheses of nucleosides of potential value as antitumor agents (page 936, left column, first paragraph). Compound II of Miller is structurally very close to that of the compound claimed in instant claim 29 except that the carbonyl group in the base is not present as an enolate. But such an enolate structure is an important intermediate as taught by Fox (above). Applicants argue that the intentional preparation of the enolate of the thymidine base such as compound 3 of Fox results in cyclization to form the tricyclic structures represented by compound 4. This is the case only if the enolate is generated and does not have another electrophilic compound to react with. In the absence of another electrophilic compound the enolate will displace the leaving group to form the tricyclic compound. One of skill in the art knows that enolates can be trapped with electrophiles to form the corresponding enol ethers such as methyl halide under appropriate reaction conditions. Since Fox or Miller does not specifically disclose such a reaction does not mean that such a reaction cannot be performed to make the enol ether as recited in instant claim 29.

Intermediate 8 taught by Fox can then be used for making derivatives with protection of the 5' or the 3' hydroxyl groups. One of skill in the art will recognize this from the teachings of Fox and Miller. Fox teaches the conversion of the anhydro intermediate 4 to the derivative 5. It

may not be the same as the compound obtained in step (c) of instant claim 1 but is similar. A derivative that is structurally similar to the compound in step (a) of claim 1 (the protected derivative) is taught by Miller (structure III of Miller in Figure 1). Even though the structure of the anhydro derivatives are slightly different in both Fox and Miller one of ordinary skill in the art will recognize that the sequence of steps can be applied to make the compound in instant claim 1 via the steps as instantly claimed with slight modifications. Such a modification based on the prior art is well within the purview of one of ordinary skill in the art.

Based on the teachings of the prior art, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make compounds as claimed in instant claims 21-30 via the process as claimed in instant claims 1-20 since structurally very close compounds as instantly claimed and steps for the same are seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make compounds as instantly claimed via the process as instantly claimed and taught by the prior art, since they serve as intermediates for the syntheses of several other derivatives having biological activity including antitumor activity as taught by Fox and Miller. Similarity in structure and function entails motivation for making the compounds as instantly claimed via the method as instantly claimed.

Obviousness based on similarity of structure and function entails motivation to make the claimed compound in expectation that compounds similar in structure will have similar properties. Where prior art compound essentially brackets the claimed compounds and are well known biologically active agents, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new agents. In re Payne, 606 F. 2d 303, 203, USPQ, 245, 254-55 (C.C.P.A. 1979).

Conclusion

Claims 1-32 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK

/Shaojia Anna Jiang, Ph.D./

Supervisory Patent Examiner, Art Unit 1623